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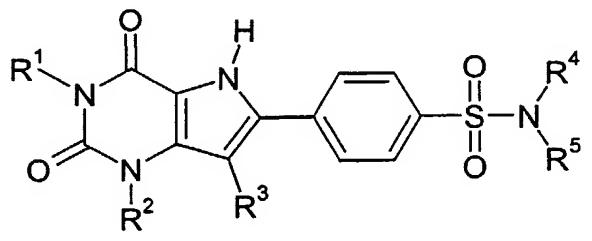
(54) Title: NEW-4-(PYRROLOPYRIMIDIN-6-YL)BENZENESULPHONAMIDE DERIVATIVES



(I)

(57) Abstract: This invention is directed to new potent and selective antagonists of A_{2A} and/or A_{2B} adenosine receptors having the general formula (I) to process for their preparation; to pharmaceutical compositions comprising them; and to their use in therapy.

NEW 4-(PYRROLOPYRIMIDIN-6-YL)BENZENESULPHONAMIDE DERIVATIVES

The present invention relates to new antagonists of A_{2A} and A_{2B} adenosine receptors. These compounds are useful in the treatment, prevention or suppression of diseases and disorders known to be susceptible of being improved by antagonism of A_{2A} and/or A_{2B} adenosine receptors, such as Parkinson's disease, asthma, allergic diseases, inflammation, atherosclerosis, hypertension, gastrointestinal tract disorders, cell proliferation disorders and autoimmune diseases.

Adenosine regulates several physiological functions through specific cell membrane receptors, which are members of the G-protein coupled receptor family. Four distinct adenosine receptors have been identified and classified: A_1, A_{2A}, A_{2B} and A_3.

A_{2A} adenosine receptors are mainly found in the brain (striatum, nucleus accumbens and olfactory bulb), platelets, leukocytes, spleen and thymus (see Fredholm et al. *Pharmacol Rev.* 2001, *53 (4)*, 527-552). Adenosine A_{2A} receptors modulate the release of GABA in the striatum. Thus, A_{2A} receptor antagonists are a useful alternative for the treatment for Parkinson´s disease (Mally, J. and Stone, T.W., *CNS Drugs*, 1998, *10*, 311-320) and for other neurodegenerative diseases. The pharmacology of A_{2A} adenosine receptors has been reviewed by Ongini et al. in *Trends Pharmacol. Sci.* 1996, *17(10)*, 364-372.

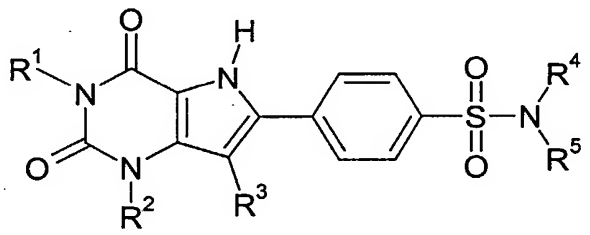
The A_{2B} adenosine receptor subtype (see Feoktistov, I., Biaggioni, I. *Pharmacol. Rev.*. 1997, *49*, 381-402) has been identified in a variety of human and murine tissues and is involved in the regulation of vascular tone, smooth muscle growth, angiogenesis, hepatic glucose production, bowel movement, intestinal secretion, and mast cell degranulation.

In view of the physiological effects mediated by adenosine receptor activation, several A_{2A} and/or A_{2B} receptor antagonists have been recentlty disclosed for the treatment or prevention of Parkinson´s disease, Alzheimer disease, Huntington chorea, Wilson's disease, asthma, bronchoconstriction, allergic diseases, hypertension, atherosclerosis, reperfusion injury, myocardial ischemia, retinopathy, inflammation, gastrointestinal tract disorders, cell proliferation diseases and/or diabetes mellitus. See for example WO 01/16134, WO 01/02400, WO 01/80893 or WO 00/73307.

It has now been found that certain 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives are new potent and selective antagonists of A_{2A} and A_{2B} adenosine receptors and can therefore be used in the treatment or prevention of these diseases.

Further objectives of the present invention are to provide a method for preparing said compounds; pharmaceutical compositions comprising an effective amount of said compounds; the use of the compounds in the manufacture of a medicament for the treatment of pathological conditions or diseases susceptible of being improved by antagonism of A_{2A} and/or A_{2B} adenosine receptors; and methods of treatment of pathological conditions or diseases susceptible to amelioration by antagonism of A_{2A} and/or A_{2B} adenosine receptors comprising the administration of the compounds of the invention to a subject in need of treatment.

Thus, the present invention is directed to new 6-(4-aminosulphonylphenyl)-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives of formula (I)



(I)

wherein

R^1 and R^2 each independently represent:

a hydrogen atom;

a hydrocarbon chain selected from an alkyl, alkenyl or alkynyl group, which is optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from halogen, hydroxy, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, cyano, oxo, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy or dialkoxyphosphoryloxy groups;

or a group of formula

$-(CH_2)_n-R^6$

wherein n is an integer from 0 to 4 and R^6 represents a 3- to 7-membered aromatic or non-aromatic cyclic group containing from 0 to 4 heteroatoms selected from N, O and S, which is optionally bridged and/or fused to another 3- to 7-membered aromatic or non-aromatic cyclic group containing from 0 to 4 heteroatoms selected from N, O and S;

the cyclic groups in the moiety R^6 being optionally substituted by one or more, for example 1, 2, 3 or 4, R^7 substituents selected from halogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, nitro, cyano, oxo, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy and dialkoxyphosphoryloxy groups;

the hydrocarbon chains and the cyclic moieties of these R^7 substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further R^8 substituents selected from halogen, hydroxy, oxo, cyano, alkyl, difluoromethyl, trifluoromethyl, alkoxy, alkylenedioxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, monoalkylamino, dialkylamino and hydroxycarbonyl groups;

R^3 represents a hydrogen or halogen atom, or a nitro, alkoxycarbonyl or alkyl group; the alkyl group being optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from hydroxy, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl or alkylcarbamoyl groups;

R^4 and R^5 are the same or different, each independently representing:

hydrogen;

a group of formula $-(CH_2)_n-R^6$, wherein n is an integer from 0 to 4; and R^6 is as defined above and is optionally substituted by one or more, for example 1, 2, 3 or 4, R^7

substituents, wherein R^7 is as defined above and is optionally substituted by one or more, for example 1, 2, 3 or 4, further R^8 substituents, wherein R^8 is as defined above;

or a hydrocarbon chain selected from alkyl, alkenyl or alkynyl, which is optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from $-(CH_2)_n-R^6$, $-O-(CH_2)_n-R^6$, $-S-(CH_2)_n-R^6$, $-NH-(CH_2)_n-R^6$, hydroxy, oxo, halogen, alkoxy, alkylthio, amino, monoalkylamino, and dialkylamino groups; the alkyl chains in the alkoxy, alkylthio, monoalkylamino and dialkylamino substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further substituents selected from $-(CH_2)_n-R^6$, hydroxy, oxo, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; and wherein each n is independently an integer from 0 to 4 and each R^6 is as defined above and is optionally substituted by one or more, for example 1, 2, 3 or 4, R^7 substituents, wherein R^7 is as defined above and is optionally substituted by one or more, for example 1, 2, 3 or 4, further R^8 substituents, wherein R^8 is as defined above;

or, alternatively, R^4 and R^5, together with the nitrogen atom to which they are attached, form a 3- to 7-membered aromatic or non-aromatic cyclic group comprising from 1 to 4 heteroatoms selected from N, O and S, which is optionally bridged and/or fused to another 3- to 7-membered aromatic or non-aromatic cyclic group containing from 0 to 4 heteroatoms selected from N, O and S; the cyclic groups being optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from $-(CH_2)_n-R^6$ and R^7; the hydrocarbon chains and the cyclic moieties of the R^7 substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further substituents selected from $-(CH_2)_n-R^6$ and R^8; and the alkyl chains in the R^8 substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further substitutents selected from $-(CH_2)_n-R^6$, hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; wherein each of the R^6 substituents is optionallly substitued by one or more, for example 1, 2, 3 or 4, R^7 substituents and each of these R^7 substituents is optionally substituted by one or more, for example 1, 2, 3 or 4, R^8 substituents; and wherein each n, R^6, R^7 and R^8 is as defined above.

or an N-oxide or a pharmaceutically acceptable salt thereof.

As used herein, a hydrocarbon chain is a straight or branched non-cyclic sequence of carbon atoms covalently linked by single, double or triple bonds, and substituted by

hydrogen atoms, for example straight or branched alkyl, alkenyl or alkynyl groups, moieties or chains. Typically, the hydrocarbon chains contain from 1 to 10 carbon atoms. As used herein, an alkyl, alkenyl or alkynyl group or moiety is a straight or branched group or moiety. Typically it is a C_1-C_{10} group or moiety, for example a C_1-C_6 group or moiety, preferably a C_1-C_4 group or moiety. Examples include methyl, ethyl, i-propyl, n-propyl, n-butyl, t-butyl, allyl, 2-propenyl and 3-butynyl. Where a group contains two or more alkyl, alkenyl or alkynyl moieties, these moieties may be the same or different. When an alkyl, alkenyl or alkynyl chain, group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, an alkylene group or moiety is a divalent alkyl moiety typically having from 1 to 6, for example from 1 to 4, carbon atoms. Examples of C_1-C_4 alkylene groups include methylene, ethylene, propylene and butylene groups. When an alkylene or alkylenedioxy group is present as a substituent on another group it shall be deemed to be a single substituent, rather than a group formed by two substituents.

As used herein, the alkyl chains present in the arylalkyl, heteroarylalkyl, alkoxy, alkylthio, monoalkylamino, dialkylamino, hydroxyalkoxy, alkoxycarbonyl, alkylcarbamoyl, alkylenedioxy and dialkoxyphosphoryloxy groups are typically straight or branched alkyl chains containing from 1 to 6 carbon atoms.

As used herein, an acyl group or moiety typically has from 2 to 7 carbon atoms. Thus, it is typically a group of formula -COR wherein R is a hydrocarbon chain group having from 1 to 6 carbon atoms. Preferably, it is a group of formula -COR wherein R is a C_1-C_6 alkyl group.

As used herein, an aryl group or moiety is typically a C_6-C_{10} aryl group or moiety such as phenyl or naphthyl. Phenyl is preferred. When an aryl group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, a heteroaryl group or moiety is typically a 5- to 10- membered aromatic ring, such as a 5- or 6- membered ring, containing at least one heteroatom selected from O, S and N. Examples include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, furanyl, oxadiazolyl, oxazolyl, imidazolyl, thiazolyl, thiadiazolyl, thienyl, pyrazolidinyl, pyrrolyl and pyrazolyl groups. Oxadiazolyl, oxazolyl, pyridyl, pyrrolyl, imidazolyl, thiazolyl, thiadiazolyl,

furanyl, thienyl, pyrazinyl and pyrimidinyl groups are preferred. When a heteroaryl group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, a cycloalkyl group typically has from 3 to 6 carbon atoms. Examples include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. It is preferably cyclopropyl, cyclopentyl or cyclohexyl. When a cycloalkyl group carries 2 or more substituents, the substituents may be the same or different.

As used herein, a heterocyclyl group is typically a non-aromatic, saturated or unsaturated C_3-C_{10} carbocyclic ring in which one or more, for example 1, 2, 3 or 4 of the carbon atoms are replaced by a heteroatom selected from N, O and S. Saturated heterocyclyl groups are preferred. Examples of suitable heterocyclyl groups include piperidinyl, piperazinyl, morpholinyl, 4,5-dihydro-oxazolyl, 3-aza-tetrahydrofuranyl, imidazolidinyl and pyrrolidinyl groups. Where a heterocyclyl group carries 2 or more substituents, the substituents may be the same or different.

As used herein, a halogen atom, is typically a chlorine, fluorine or bromine atom.

As used herein, some of the atoms, groups, moieties, chains or cycles present in the general structures of the invention are "optionally substituted". This means that these atoms, groups, moieties, chains or cycles can be either unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents, whereby the hydrogen atoms bound to the unsubstituted atoms, groups, moieties, chains or cycles are replaced by chemically acceptable atoms, groups, moieties, chains or cycles. Typically when a cyclic group is bridged by an alkylene group, the bridging alkylene group is attached to the ring at non-adjacent atoms.

Compounds of the formula (I) containing one or more chiral centre may be used in enantiomerically or diastereoisomerically pure form, or in the form of a mixture of isomers.

As used herein, a pharmaceutically acceptable salt is a salt with a pharmaceutically acceptable acid or base. Pharmaceutically acceptable acids include both inorganic acids, for example hydrochloric, sulphuric, phosphoric, diphosphoric, hydrobromic and nitric acid and organic acids, for example citric, fumaric, maleic, malic, ascorbic, succinic, tartaric, benzoic, acetic, methanesulphonic, ethanesulphonic, benzenesulphonic or p-

toluenesulphonic acid. Pharmaceutically acceptable bases include alkali metal (e.g. sodium or potassium) and alkali earth metal (e.g. calcium or magnesium) hydroxides and organic bases, for example alkyl amines, aralkyl amines and heterocyclic amines.

As used herein, an N-oxide is formed from the tertiary basic amines or pyridines present in the molecule, using a convenient oxidising agent.

Preferred compounds of the invention are those wherein R^1 and R^2 are independently an alkyl group optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, hydroxycarbonyl, and alkoxycarbonyl groups; or a group of formula $-(CH_2)_n-R^6$, wherein n is an integer from 0 to 2 and R^6 represents a 3- to 7-membered aromatic or non-aromatic cyclic group having from 0 to 2 heteroatoms selected from nitrogen and oxygen. More preferred compounds are those wherein the alkyl chains, moieties or groups present R^1 and R^2 are C_1-C_6 alkyl chains, moieties or groups. Most preferably, R^1 and R^2 are both unsubstituted C_1-C_6 alkyl groups.

Further preferred compounds of the invention are those wherein R^3 represents hydrogen or a halogen atom, more preferably hydrogen or a chlorine atom, most preferably hydrogen.

Also preferred are compounds wherein R^4 is as defined above and R^5 is hydrogen, a group of formula $-(CH_2)_n-R^6$ or a hydrocarbon chain selected from alkyl, alkenyl and alkynyl, which is optionally substituted by one or more, for example 1, 2, 3 or 4, groups selected from $-(CH_2)_n-R^6$ and $-(CH_2)_n-O-R^6$; each R^6 being a phenyl or a pyridyl group, which is optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from halogen, hydroxy, alkyl, alkoxy and alkylthio groups. More preferred compounds are those wherein R^5 is hydrogen, alkyl or benzyl. Most preferred compounds are those wherein R^5 is hydrogen or alkyl.

Typically, R^4 is:

- hydrogen;

- a group of formula $-(CH_2)_n-R^6$, wherein n is 0, 1 or 2 and R^6 is a 5- to 7-membered aromatic or non-aromatic cyclic group containing 0 to 2 heteroatoms selected from N, O and S, which is optionally substituted by one or more, for example 1, 2, 3 or 4, R^7 substituents selected from halogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, nitro, cyano, oxo, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy and dialkoxyphosphoryloxy groups; the hydrocarbon chains and the cyclic moieties of these R^7 substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further R^8 substituents selected from halogen, hydroxy, oxo, cyano, alkyl, trifluoromethyl, alkoxy, alkylenedioxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, monoalkylamino, dialkylamino and hydroxycarbonyl groups; or

- an alkyl, alkenyl or alkynyl chain, which is optionally substituted by one or more, for example 1, 2, 3 or 4, substituents selected from $-(CH_2)_n-R^6$, $-O-(CH_2)_n-R^6$, $-S-(CH_2)_n-R^6$, $-NH-(CH_2)_n-R^6$, hydroxy, oxo, halogen, alkoxy, alkylthio, amino, monoalkylamino, and dialkylamino groups; the alkyl chains in the alkoxy, alkylthio, monoalkylamino and dialkylamino substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further substituents selected from $-(CH_2)_n-R^6$, hydroxy, oxo, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; and wherein each n is independently an integer from 0 to 4 and each R^6 is is independently a 5- or 6-membered aromatic or non-aromatic cyclic group having 0, 1 or 2 heteroatoms selected from N, O and S, and is optionally substituted by one or more, for example 1, 2, 3 or 4, R^7 substituents, wherein R^7 is as defined above and is optionally substituted by one or more, for example 1, 2, 3 or 4, further R^8 substituents, wherein R^8 is as defined above;

More preferably, R^4 is:

- hydrogen;

- a group of formula $-(CH_2)_n-R^6$ wherein n is 0, 1 or 2 and R^6 is a 5- to 6- membered heteroaryl or heterocyclyl group containing up to 2 heteroatoms selected from N, O and S, for example a piperidinyl, pyrrolidinyl or pyridyl group, which is optionally substituted by a R^7 substituent selected from halogen, alkyl, alkoxy, arylalkyl or heteroarylalkyl groups, the

aryl and heteroaryl moieties of these arylalkyl and heteroarylalkyl R^7 substituents being optionally substituted by 1 or 2 further R^8 substituents selected from halogen, cyano, alkyl, trifluoromethyl, alkoxy and alkylenedioxy; or

- an alkyl group which is optionally substituted by 1 or 2 substituents selected from amino, monoalkylamino, dialkylamino, $-OR^6$ and $-SR^6$ substituents, wherein R^6 is a 5- or 6-membered heteroaryl group containing 1 or 2 heteroatoms, for example a pyridyl group, and is optionally substituted by one or more R^7 substituents selected from hydroxy, halogen, amino, monoalkylamino, dialkylamino, cyano, hydroxycarbonyl, alkoxycarbonyl, alkoxy, alkylenedioxy and alkylthio; and wherein the alkyl chains of each of the said monoalkylamino and dialkylamino substituents are optionally substituted by 1 or 2 further substituents selected from a hydroxy group and a group of formula $-(CH_2)_n-R^6$, wherein n is an integer from 0 to 4 and R^6 is an aryl group, for example a benzyl group.

Most preferably, R^4 is:

- a group of formula $-(CH_2)_n-R^6$ wherein n is 0, 1 or 2 and R^6 is a 5- to 6- membered heteroaryl or heterocyclyl group containing up to 2 N atoms, for example a piperidinyl, pyrrolidinyl or pyridyl group, which is optionally substituted by a R^7 substituent selected from halogen, alkyl, alkoxy, arylalkyl or heteroarylalkyl groups, the aryl and heteroaryl moieties of these arylalkyl and heteroarylalkyl R^7 substituents being optionally substituted by 1 or 2 further R^8 substituents selected from halogen and alkoxy; or
- an alkyl group which is optionally substituted by 1 or 2 substituents selected from monoalkylamino, dialkylamino, $-OR^6$ and $-SR^6$ substituents, wherein R^6 is a 5- or 6-membered heteroaryl group containing 1 or 2 N atoms, for example a pyridyl group, and is optionally substituted by one or more R^7 substituents selected from halogen and alkoxy; and wherein the alkyl chains of each of the said monoalkylamino and dialkylamino substituents are optionally substituted by 1 or 2 further substituents selected from a hydroxy group and a group of formula $-(CH_2)_n-R^6$, wherein n is an integer from 0 to 4 and R^6 is an aryl group, for example a benzyl group.

In other preferred embodiments of the invention R^4 and R^5 form, together with the nitrogen atom to which they are attached, an optionally bridged 5- to 7-membered aromatic or non-aromatic cyclic group which contains up to two nitrogen atoms, and which is optionally substituted by a group of formula $-(CH_2)_n-R^6$ or by a R^7 substituent selected from alkyl, alkenyl and alkynyl chains; the said alkyl, alkenyl and alkynyl chains being optionally

substituted by one or more, for example 1, 2, 3 or 4, groups of formula $-(CH_2)_n-R^6$ or R^8 substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino, and dialkylamino groups; the alkyl chains in these R^8 substituents being optionally substituted by one or more, for example 1, 2, 3 or 4, further substituents selected from a group of formula $-(CH_2)_n-R^6$, and hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; wherein each of the R^6 groups is optionallly substitued by one or more, for example 1, 2, 3 or 4, R^7 substituents and each of these R^7 substituents is optionally substituted by one or more, for example 1, 2, 3 or 4, R^8 substituents; each n, R^6, R^7 and R^8 being as defined above.

More preferably, R^4 and R^5 form, together with the N atom to which they are attached, a 5-, 6- or 7- membered saturated heterocyclic group which contains 1 or 2 nitrogen atoms and which optionally carries a bridging alkylene group (for example a piperazinyl, homopiperazinyl, or 2,5-methanopiperazinyl group), said cyclic group being optionally substituted by a group of formula $-(CH_2)_n-R^6$ wherein n is 0, 1 or 2 and R^6 is a 5- or 6-membered aromatic or non-aromatic ring containing 0, 1 or 2 heteroatoms selected from N, O and S (for example, a phenyl, furanyl, thienyl, pyridyl or pyrimidinyl ring), or by a R^7 substituent selected from alkyl and alkenyl groups, the group R^6 being optionally substituted by 1, 2 or 3 further substituents selected from haloalkyl, alkyl, alkoxy, alkylenedioxy, cyano and halogen groups, and the said R^7 substituent being optionally substituted by 1 or 2 phenyl substituents.

Particular individual compounds of the invention include:

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2,4-Difluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{4-[4-(2-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[4-(4-trifluoromethylbenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-*tert*-Butylbenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-{4-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl]piperazin-1-ylmethyl}benzonitrile

6-[4-(4-Furan-3-ylmethylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-[4-(4-thiophen-2-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-[4-(4-pyridin-4-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[4-(1-phenylethyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzyl-[1,4]diazepane-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)[1,4]diazepane-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[4-((*E*)-3-phenylallyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-((1*S*,4*S*)-5-Benzyl-2,5-diazabicyclo[2.2.1]heptane-2-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzhydrylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-[2-(Benzylmethylamino)ethyl]-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

1,3-Dimethyl-6-[4-(4-pyridin-2-yl-piperazine-1-sulphonyl)-phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Methoxypyrimidin-4-yl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[1-(4-fluorobenzyl)piperidin-4-yl]benzenesulphonamide

N-[1-(3,4-Dimethoxybenzyl)piperidin-4-yl]-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(1-thiophen-2-ylmethylpiperidin-4-yl)benzenesulphonamide

N-(1-Benzylpiperidin-4-yl)-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methylbenzenesulphonamide

N-(1-Benzylpyrrolidin-3-yl)-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-(1-Benzylpyrrolidin-3-yl)-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methylbenzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(6-methoxypyridin-3-yl)benzenesulphonamide,

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylbenzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(5-methylpyridin-2-yl)benzenesulphonamide

1,3-Dimethyl-6-[4-(4-phenylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[4-(4-trifluoromethylphenyl)piperazine-1-sulphonyl]-phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3,5-Dichloropyridin-4-yl)-piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(4-fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(3-fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2,4-Difluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(4-trifluoromethylbenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-*tert*-Butylbenzyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(4-methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(3-methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-{4-[4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl]piperazin-1-ylmethyl}benzonitrile

1,3-Diethyl-6-[4-(4-furan-2-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-[4-(4-thiophen-2-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-[4-(4-pyridin-4-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(1-phenylethyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-{4-[4-(4-fluorobenzyl)-[1,4]diazepane-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Diethyl-6-[4-(4-phenethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-((1*S*,4*S*)-5-Benzyl-2,5-diazabicyclo[2.2.1]heptane-2-sulphonyl)phenyl]-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-[2-(Benzylmethylamino)ethyl]-4-(diethyldioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-{2-[Benzyl-(2-hydroxyethyl)amino]ethyl}-4-(diethyldioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

1,3-Diethyl-6-[4-(4-pyridin-2-ylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(1,3-diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[1-(4-fluorobenzyl)piperidin-4-yl]benzenesulphonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[1-(3,4-dimethoxybenzyl)piperidin-4-yl]benzenesulphonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(1-thiophen-2-ylmethylpiperidin-4-yl)benzenesulphonamide

N-(1-Benzylpiperidin-4-yl)-4-(1,3-diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methylbenzenesulphonamide

N-(1-Benzylpyrrolidin-3-yl)-4-(1,3-diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-(1-Benzylpyrrolidin-3-yl)-4-(1,3-diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-N-methylbenzenesulphonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-yl-ethyl)benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-dipropyl-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2,4-Difluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dipropyl-6-{4-[4-(4-trifluoromethylbenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-*tert*-Butylbenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-{4-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl]piperazin-1-ylmethyl}benzonitrile

1,3-Dipropyl-6-[4-(4-thiophen-2-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dipropyl-6-[4-(4-pyridin-4-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(1-Phenylethyl)piperazine-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)-[1,4]diazepane-1-sulphonyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Phenethylpiperazine-1-sulphonyl)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dipropyl-6-[4-(4-pyridin-2-ylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[1-(4-fluorobenzylpiperidin-4-yl]benzenesulphonamide

N-[1-(3,4-Dimethoxybenzyl)piperidin-4-yl]-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(1-thiophen-2-yl-methylpiperidin-4-yl)benzenesulphonamide

N-(1-Benzylpiperidin-4-yl)-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methylbenzenesulphonamide

N-(1-Benzylpyrrolidin-3-yl)-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(6-methoxypyridin-3-yl)benzenesulphonamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-yl-ethyl)benzenesulphonamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylbenzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2,4-Difluorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1-Methyl-3-propyl-6-{4-[4-(4-trifluoromethylbenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-*tert*-Butylbenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-{4-[4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl]piperazin-1-ylmethyl}benzonitrile

6-[4-(4-Furan-3-ylmethylpiperazine-1-sulphonyl)phenyl]-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1-Methyl-3-propyl-6-[4-(4-thiophen-2-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1-Methyl-3-propyl-6-[4-(4-pyridin-4-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)-[1,4]diazepane-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-[2-(Benzylmethylamino)ethyl]-4-(methyldioxopropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

1-Methyl-3-propyl-6-[4-(4-pyridin-2-ylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)benzenesulphonamide

N-[1-(4-Fluoro-benzyl)piperidin-4-yl]-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-[1-(3,4-Dimethoxybenzyl)piperidin-4-yl]-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(1-thiophen-2-ylmethylpiperidin-4-yl)benzenesulphonamide

N-(1-Benzylpiperidin-4-yl)-*N*-methyl-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Chlorobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(2-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

3-Methyl-1-propyl-6-{4-[4-(4-trifluoromethylbenzyl)piperazine-1-sulphonyl]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-*tert*-Butylbenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Methoxybenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-{4-[4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl]piperazin-1-ylmethyl}benzonitrile

3-Methyl-1-propyl-6-[4-(4-thiophen-2-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]-phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

3-Methyl-1-propyl-6-[4-(4-pyridin-4-ylmethylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

3-Methyl-6-{4-[4-(1-phenylethyl)piperazine-1-sulphonyl]-phenyl}-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzyl[1,4]diazepane-1-sulphonyl)phenyl]-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)[1,4]diazepane-1-sulphonyl]-phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

3-Methyl-6-[4-(4-phenethylpiperazine-1-sulphonyl)phenyl]-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(5-Benzyl-2,5-diazabicyclo[2.2.1]heptane-2-sulphonyl)-phenyl]-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-[2-(Benzylmethylamino)ethyl]-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-{2-[Benzyl-(2-hydroxyethyl)amino]ethyl}-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

3-Methyl-1-propyl-6-[4-(4-pyridin-2-yl-piperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-[1-(4-Fluorobenzyl)-piperidin-4-yl]-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

N-[1-(3,4-Dimethoxybenzyl)piperidin-4-yl]-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(1-thiophen-2-ylmethylpiperidin-4-yl)benzenesulphonamide

N-(1-Benzylpiperidin-4-yl)-*N*-methyl-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-yl-ethyl)benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-7-chloro-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylmethylbenzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-3-ylmethylbenzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-4-ylmethylbenzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(6-methoxypyridin-3-ylmethyl)benzenesulfonamide

N-(3-Chloropyridin-4-ylmethyl)-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methyl-*N*-(2-pyridin-2-ylethyl)benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-3-ylethyl)benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-4-ylethyl)benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(6-methoxypyridin-2-yloxy)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(4-methylpyridin-2-yloxy)ethyl]benzenesulfonamide

N-[2-(5-Chloropyridin-2-yloxy)ethyl]-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(5-trifluoromethylpyridin-2-yloxy)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-3-yloxy)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyrazin-2-yloxy)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-ylsulfanyl)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyrimidin-2-ylsulfanyl)ethyl]benzenesulfonamide

N-Benzyl-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide

N-Benzyl-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(6-methoxypyridin-2-yloxy)ethyl]benzenesulfonamide

N-Benzyl-*N*-[2-(6-chloropyridin-3-yloxy)ethyl]-4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulfonamide

6-[4-(4-Benzylpiperidine-1-sulfonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Methoxyphenyl)piperidine-1-sulfonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylmethylbenzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-3-ylmethylbenzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-4-ylmethylbenzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(6-methoxypyridin-3-ylmethyl)benzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methyl-*N*-(2-pyridin-2-ylethyl)benzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-3-ylethyl)benzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-4-ylethyl)benzenesulfonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-3-yloxy)ethyl]benzenesulfonamide

N-Benzyl-4-(1,3-diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-methyl-*N*-(2-pyridin-2-yl-ethyl)benzenesulfonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylmethylbenzenesulfonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-3-ylmethylbenzenesulfonamide

N-(6-Methoxypyridin-3-ylmethyl)-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulfonamide

N-Methyl-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulfonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-3-ylethyl)benzenesulfonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-4-ylethyl)benzenesulfonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide

N-Benzyl-4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylmethylbenzenesulfonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-3-ylmethylbenzenesulfonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-4-ylmethylbenzenesulfonamide

N-(6-Methoxypyridin-3-ylmethyl)-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulfonamide

N-(3-Chloropyridin-4-ylmethyl)-4-(3-methyl-2,4-dioxo-1 -propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulfonamide

N-Methyl-4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulfonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-3-yl-ethyl)benzenesulfonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-4-ylethyl)benzenesulfonamide

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)-ethyl]benzenesulfonamide

1,3-Dimethyl-6-[4-(2,3,5,6-tetrahydro-[1,2']bipyrazinyl-4-sulfonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1-Ethyl-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d] pyrimidin-6-yl)-N-pyridin-2-ylmethyl-benzenesulfonamide

4-(1-Ethyl-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d] pyrimidin-6-yl)-N-(2-pyridin-2-ylethyl)-benzenesulfonamide

4-(1-Ethyl-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d] pyrimidin-6-yl)-N-[2-(pyridin-2-yloxy)ethyl]-benzenesulfonamide

4-(1-Ethyl-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d] pyrimidin-6-yl)-N-(6-methoxy-pyridin-3-ylmethyl)-benzenesulfonamide

4-[1,3-Bis-(3-methoxypropyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]-*N*-pyridin-3-ylmethylbenzenesulphonamide

6-{4-[4-(4-Bromobenzyl)-piperazine-1-sulphonyl]phenyl}-1,3-bis-(2-methoxyethyl)-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-[1,3-Bis-(2-methylsulphanylethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]-N-pyridin-4-ylmethylbenzenesulphonamide

6-{4-[4-(4-Bromobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-bis-(2-methylsulphanyl-ethyl)-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

{4-[4-(4-Bromobenzyl)-piperazine-1-sulphonyl]phenyl}-3-methyl-1-pyridin-4-ylmethyl-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-Methyl-4-(3-methyl-2,4-dioxo-1-pyridin-4-ylmethyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-yl-ethyl)benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-3-methyl-1-phenethyl-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(3-Methyl-2,4-dioxo-1-phenethyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylmethylbenzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-bis-cyclopropylmethyl-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1,3-Bis-cyclopropylmethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-3-yl-ethyl)benzenesulphonamide

4-[2,4-Dioxo-1,3-bis-(2,2,2-trifluoroethyl)-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]-*N*-(6-methoxypyridin-3-ylmethyl)benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-bis-(2,2,2-trifluoroethyl)-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(6-Methoxypyridin-3-ylmethyl)-4-[3-methyl-1-(2-morpholin-4-yl-ethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-3-methyl-1-(2-morpholin-4-ylethyl)-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1-Benzyl-6-{4-[4-(4-bromobenzyl)piperazine-1-sulphonyl]phenyl}-3-methyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1-Benzyl-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulphonamide

3-{6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-pyrrolo[3,2-*d*]pyrimidin-1-yl}propionic acid methyl ester

4-[1-(3-Hydroxypropyl)-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulphonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1-cyclopentyl-3-methyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1-Cyclopentyl-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-4-yl-ethyl)benzenesulphonamide

Of outstanding interest are:

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(6-methoxypyridin-2-yloxy)ethyl]benzenesulfonamide

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(4-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1-Methyl-3-propyl-6-[4-(4-pyridin-2-ylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulphonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylbenzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(6-methoxypyridin-3-yl)benzenesulphonamide

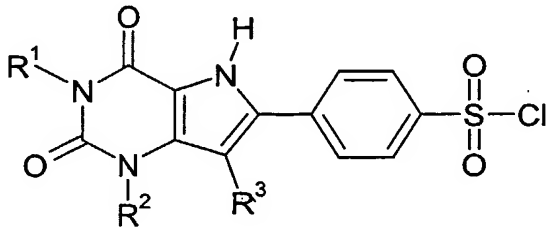
6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

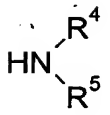
4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[1-(4-fluorobenzyl)piperidin-4-yl]benzenesulphonamide

According to a further feature of the present invention, the 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of general formula (I) are prepared by reaction of the corresponding sulphonyl chloride of formula (II):



(II)

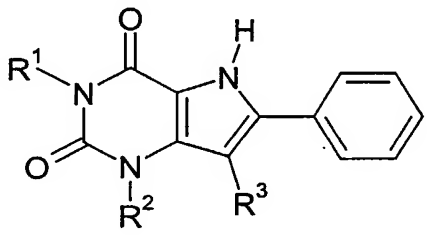
(wherein R^1, R^2 and R^3 are as hereinbefore defined) and the corresponding amine (III):



(III)

(wherein R^4 and R^5 are as hereinbefore defined). The reaction is carried out in an organic solvent, preferably a polar aprotic organic solvent such as dioxane, methylene chloride or tetrahydrofuran, at a temperature from 10°C to 40°C and in the presence of an organic base, preferably an amine base such as triethylamine or polymer supported morpholine. The thus obtained 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivative is then isolated by standard methods known in the art.

When R^3 is hydrogen, the sulphonyl chloride of formula (II) is obtained from the corresponding compound of formula (IV):



(IV)

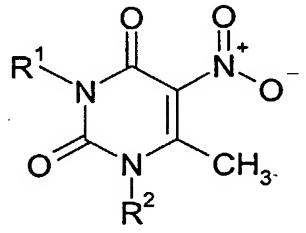
(wherein R^1, R^2 and R^3 are as hereinbefore defined), by reaction with an excess of chlorosulphonic acid and optionally thionyl chloride, preferably under a nitrogen atmosphere and at a temperature from –5°C to 10°C.

When R^3 is a chlorine atom, the sulphonyl chloride of formula (II) is obtained from the corresponding compound of formula (IV) by reaction with a mixture of chlorosulphonic acid and sulphuryl chloride, preferably under a nitrogen atmosphere and at a temperature from –5°C to 10°C.

When R^3 is a bromine or an iodine atom, the sulphonyl chloride of formula (II) is obtained from the corresponding sulphonyl chloride of formula (II) where R^3 is a hydrogen atom by reaction with bromine or iodine monochloride in glacial acetic acid at room temperature.

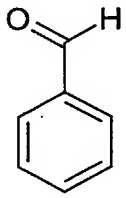
Other substitutions at R^3 can be introduced by reaction of the corresponding compounds of the general formulae (II) or (IV), or a protected version of them, with an appropiate electrophile.

The 6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives of formula (IV) can be prepared by reaction of the corresponding 6-methyl-5-nitrouracils (V):



(V)

(wherein R^1 and R^2 are as hereinbefore defined), and benzaldehyde (VI):



(VI)

followed by reductive cyclisation of the resulting 5-nitro-6-styryluracils by methods known in the art, e.g. C. E. Müller et al., *J. Med. Chem.* 1994, *37*, 1526-1534 and references cited therein.

When the defined groups R^1 to R^5 are susceptible to chemical reaction under the conditions of the hereinbefore described processes or are incompatible with said processes, alternative processes can be readily carried out utilising organic synthetic chemistry methods to, for example, protect functional groups and finally eliminate protecting groups.

The 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of formula (I) can be converted by methods known *per se* into pharmaceutically acceptable salts or N-oxides.

Preferred salts are acid addition salts obtainable by treatment with organic or inorganic acids such as fumaric, tartaric, succinic or hydrochloric acid. Also 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of formula (I) in which there is the presence of an acidic group may be converted into pharmacologically acceptable salts by reaction with an alkali metal hydroxide or an organic base such as sodium or potassium hydroxide. The acid or alkali addition salts so formed may be interchanged with suitable pharmaceutically acceptable counter ions using processes known *per se*.

Adenosine 2B receptor subtype competition radioligand binding

Human membranes from recombinant A_{2B} receptors were purchased from Receptor Biology, Inc.(USA).

Competition assays were carried out by incubation of membranes from hA_{2B} receptors transfected to HEK293 cells, [^{3}H]DPCPX as radioligand, buffer (50mM Tris-HCl (pH 6.5), 10mM $MgCl_2$, 1mM EDTA, 0.1mM benzamidine, 2units/ml adenosine deaminase), and unlabelled ligand in a total volume of 0.1 ml for 30 min at 25°C. NECA was used to determinate non-specific binding. Filter over Schleicher&Schuell GF/52 filters (pre-soaked 0.5% polyethylenyimine) in a Brandel cell harvester. Unbound radioligand was removed with 4x2 ml ice-cold 50 mM Tris-Hcl (pH 6.5).

Adenosine 2A receptor subtype competition radioligand binding

Human membranes from recombinant A_{2A} receptors were purchased from Receptor Biology, Inc.(USA).

Competition assays were carried out by incubation of membranes from hA_{2A} receptors transfected to HEK293 cells, [^{3}H]ZM241385 as radioligand, buffer (50mM Tris-HCl (pH 7.4), 10mM $MgCl_2$, 1mM EDTA, 2units/ml adenosine deaminase), and unlabelled ligand in a total volume of 0.2 ml for 90 min at 25°C. NECA was used to determinate non-specific binding. Filter over Schleicher&Schuell GF/52 filters (pre-soaked 0.5% polyethylenyimine) in a Brandel cell harvester. Unbound radioligand was removed with 3x3 ml ice-cold 50 mM Tris-Hcl 50 (pH 7.4), 0.9% NaCl.

The results are shown in Table 1 and Table 2.

TABLE 1

Example	IC_{50} A_{2B} (nM)
172	17
173	5
1	16
107	9
118	6
3	7
126	12
37	14
132	17
38	12
36	18
18	4

It can be seen from Table 1 that the compounds of formula (I) are potent inhibitors of the A_{2B} adenosine receptor subtype. Preferred 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of the invention possess an IC_{50} value for the inhibition of A_{2B} (determined as defined above) of less than 50 nM, preferably less than 20 nM and most preferably less than 10 nM.

TABLE 2

Example	IC_{50} A_{2A} (nM)
18	85
59	28
38	75
97	60
69	84

It can be seen from Table 2 that the compounds of formula (I) are potent inhibitors of the A_{2A} adenosine receptor subtype. Some preferred 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of the invention possess an IC_{50} value for the inhibition of A_{2A} (determined as defined above) of less than 100 nM and most preferably less than 50 nM.

The 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of the invention are useful in the treatment or prevention of diseases known to be susceptible to improvement by treatment with an antagonist of A_{2A} and/or A_{2B} adenosine receptors. For example (see WO 01/16134, WO 01/02400, WO 01/80893 or WO 00/73307), Parkinson's disease, Alzheimer's disease, Huntington chorea, Wilson's disease, asthma, bronchoconstriction, allergic diseases, inflammation, reperfusion injury, myocardial ischemia, atherosclerosis, hypertension, retinopathy, diabetes mellitus, inflammation, gastrointestinal tract disorders, and/or autoimmune diseases. Examples of autoimmune diseases which can be treated or prevented using the compounds of the invention are Addison's disease, autoimmune hemolytic anemia, Crohn's disease, Goodpasture's syndrome, Graves disease, Hashimoto's thyroiditis, idiopathic thrombocytopenic purpura, insulin-dependent diabetes mellitus, multiple sclerosis, myasthenia gravis, pemphigus vulgaris, pernicious anemia, poststreptococcal glomerulonephritis, psoriasis, rheumatoid arthritis, scleroderma, Sjogren's syndrome, spontaneous infertility, and systemic lupus erythematosus.

Accordingly, the 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivatives of the invention and pharmaceutically acceptable salts thereof, and pharmaceutical compositions comprising such compound and/or salts thereof, may be used in a method of treatment of disorders of the human body which comprises administering to a subject requiring such treatment an effective amount of a 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivative of the invention or a pharmaceutically acceptable salt thereof.

The present invention also provides pharmaceutical compositions which comprise, as an active ingredient, at least a 4-(pyrrolopyrimidin-6-yl)benzenesulphonamide derivative of formula (I) or a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable excipient such as a carrier or diluent. The active ingredient may comprise 0.001% to 99% by weight, preferably 0.01% to 90% by weight of the composition depending upon the nature of the formulation and whether further dilution is to be made prior to application. Preferably the compositions are made up in a form suitable for oral, topical, nasal, rectal, percutaneous or injectable administration.

The pharmaceutically acceptable excipients which are admixed with the active compound, or salts of such compound, to form the compositions of this invention are well-known *per*

se and the actual excipients used depend *inter alia* on the intended method of administering the compositions.

Compositions of this invention are preferably adapted for injectable and *per os* administration. In this case, the compositions for oral administration may take the form of tablets, retard tablets, sublingual tablets, capsules, inhalation aerosols, inhalation solutions, dry powder inhalation, or liquid preparations, such as mixtures, elixirs, syrups or suspensions, all containing the compound of the invention; such preparations may be made by methods well-known in the art.

The diluents which may be used in the preparation of the compositions include those liquid and solid diluents which are compatible with the active ingredient, together with colouring or flavouring agents, if desired. Tablets or capsules may conveniently contain between 2 and 500 mg of active ingredient or the equivalent amount of a salt thereof.

The liquid composition adapted for oral use may be in the form of solutions or suspensions. The solutions may be aqueous solutions of a soluble salt or other derivative of the active compound in association with, for example, sucrose to form a syrup. The suspensions may comprise an insoluble active compound of the invention or a pharmaceutically acceptable salt thereof in association with water, together with a suspending agent or flavouring agent.

Compositions for parenteral injection may be prepared from soluble salts, which may or may not be freeze-dried and which may be dissolved in pyrogen free aqueous media or other appropriate parenteral injection fluid.

Effective doses are normally in the range of 2-2000 mg of active ingredient per day. Daily dosage may be administered in one or more treatments, preferably from 1 to 4 treatments, per day.

The syntheses of the compounds of the invention and of the intermediates for use therein are illustrated by the following Examples (including Preparation Examples (Preparations 1-12)) which do not limit the scope of the invention in any way.

^{1}H Nuclear Magnetic Resonance Spectra were recorded on a Varian Gemini 300 spectrometer. Melting points were recorded using a Perkin Elmer DSC-7 apparatus. The chromatographic separations were obtained using a Waters 2690 system equipped with a Symmetry C18 (2.1 x 10 mm, 3.5 μM) column. As detectors a Micromass ZMD mass spectrometer using ES ionization and a Waters 996 Diode Array detector were used. The mobile phase was formic acid (0.46 ml), ammonia (0.115 ml) and water (1000 ml) (A) and formic acid (0.4 ml), ammonia (0.1 ml), methanol (500 ml) and acetonitrile (500 ml) (B): initially from 0% to 95% of B in 20 min, and then 4 min. with 95% of B. The reequilibration time between two injections was 5 min. The flow rate was 0.4 ml/min. The injection volume was 5 μl. Diode array chromatograms were processed at 210 nm.

PREPARATION EXAMPLES

PREPARATION 1

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-benzenesulphonyl chloride

a) A mixture of 1,3,6-trimethyl-5-nitro-1*H*-pyrimidine-2,4-dione (3.00 g, 15.06 mmol), benzaldehyde (1.58 ml, 15.56 mmol), piperidine (1.41 ml, 15.56 mmol) and a 3Å molecular sieve (6.00 g) in ethanol (70 ml) was refluxed for 4 hours, filtered and the solid was treated with a mixture of chloroform and methanol. The resulting suspension was filtered again and the filtrates were evaporated. The residue was triturated with diethyl ether and the precipitate collected by filtration and dried under vacuum to yield 1,3-dimethyl-5-nitro-6-((*E*)-styryl)-1*H*-pyrimidine-2,4-dione (2.61 g, 60%) as a yellow solid.

b) To a stirred solution of the above compound (2.61 g, 9.08 mmol) in formic acid (80 ml) was slowly added sodium dithionite (9.30 g, 45.42 mmol) and the mixture was refluxed overnight. The resulting mixture was cooled to room temperature and it was poured into water. The precipitate was collected by filtration, washed with water and dichloromethane and then dried under vacuum to yield 1,3-dimethyl-6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione (1.54 g, 66%) as a white solid.

c) The above compound (500mg, 1.96 mmol) was added portionwise to a mixture of chlorosulphonic acid (2.5 ml) and thionyl chloride (0.25 ml) and stirred at 0^{o} C for 1 hour

and then at room temperature for 1h 30 min. The reaction mixture was carefully poured into stirred ice-water and the resulting precipitate was collected by filtration, washed with water and diethyl ether and then dried under vacuum to yield the title product (607 mg, 88%) as a yellow solid.

^{1}H-NMR δ(DMSO): 12.5 (s, 1H), 7.9 (d, 2H), 7.6 (d, 2H), 6.8 (s, 1H), 3.5 (s, 3H), 3.3 (s, 3H).

PREPARATION 2

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl chloride

Obtained as a yellow solid (29% overall) from 1,3-diethyl-6-methyl-5-nitro-1*H*-pyrimidine-2,4-dione following the procedure described in Preparation 1.

^{1}H-NMR δ(DMSO): 12.4 (s, 1H), 7.9 (d, 2H), 7.8 (d, 2H), 6.8 (s, 1H), 3.9 (m, 4H), 1.2 (dt, 6H).

PREPARATION 3

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl chloride

Obtained as a yellow solid (18% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H*-pyrimidine-2,4-dione following the procedure described in Preparation 1.

^{1}H-NMR δ(DMSO): 12.2 (s, 1H), 7.9 (d, 2H), 7.6 (d, 2H), 6.8 (s, 1H), 3.9 (m, 4H), 1.6 (m, 4H), 0.9 (m, 6H).

PREPARATION 4

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl chloride

Obtained as a yellow solid (50% overall) from 1,6-dimethyl-5-nitro-3-propyl-1*H*-pyrimidine-2,4-dione following the procedure described in Preparation 1.

^{1}H-NMR δ(DMSO): 12.4 (s, 1H), 7.9 (d, 2H), 7.6 (d, 2H), 6.65 (s, 1H), 3.9 (t, 2H), 3.4 (s, 3H), 1.6 (m, 2H), 0.9 (t, 3H).

PREPARATION 5

4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl chloride

Obtained as a yellow solid (40% overall) from 3,6-dimethyl-5-nitro-1-propyl-1*H*-pyrimidine-2,4-dione following the procedure described in Preparation 1.

^{1}H-NMR δ(DMSO): 12.4 (s, 1H), 7.9 (d, 2H), 7.6 (d, 2H), 5.8 (s, 1H), 3.85 (t, 2H), 3.35 (s, 3H), 1.7 (m, 2H), 0.9 (t, 3H).

PREPARATION 6

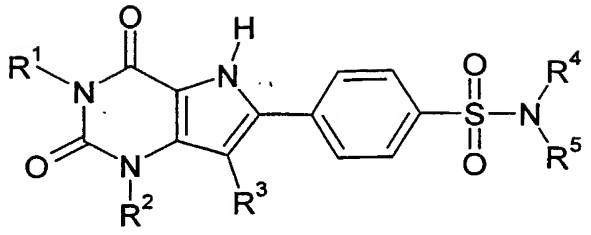
4-(7-Chloro-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonyl chloride

The title compound of Preparation 1 (600 mg,1.69 mmol) was suspended in glacial acetic acid (6 ml), sulphuryl chloride was added dropwise (205 µl, 2.54 mmol) and the mixture was stirred at room temperature for 3 hours. The reaction mixture was then filtered, washed with dietyhl ether and dried to yield the title product as a yellow solid (384 mg, 58%).

^{1}H-NMR δ(DMSO): 12.9 (s, 1H), 7.6 (m, 4H), 3.7 (s, 3H), 3.2 (s, 3H).

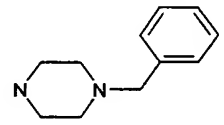
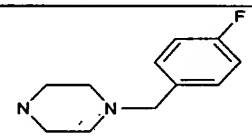
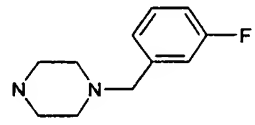
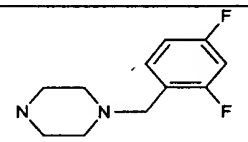
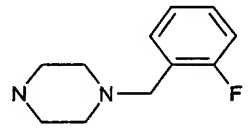
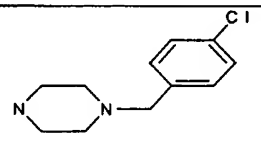
EXAMPLES

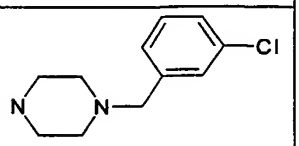
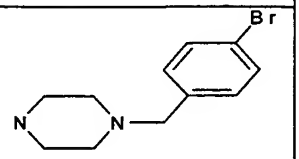
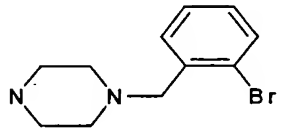
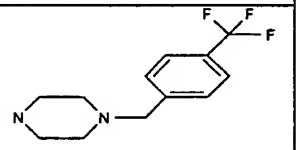
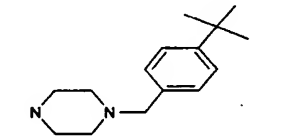
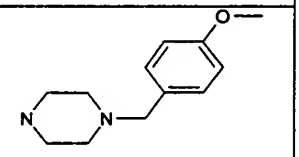
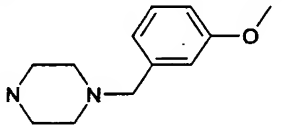
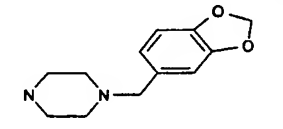
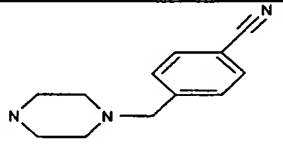
TABLE 3

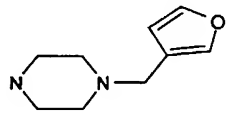
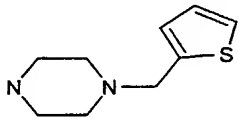
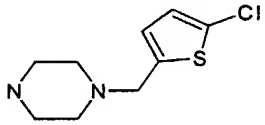
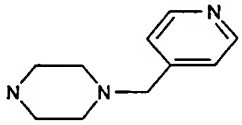
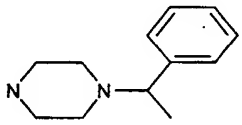
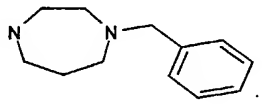
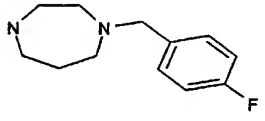
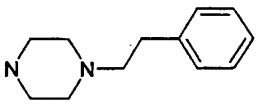
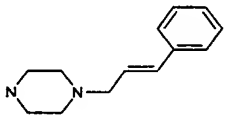


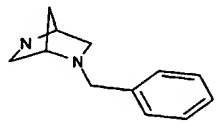
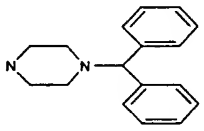
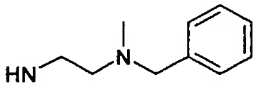
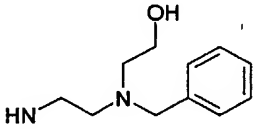
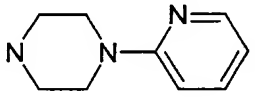
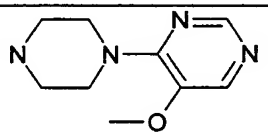
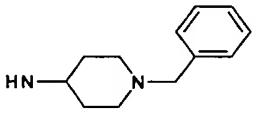
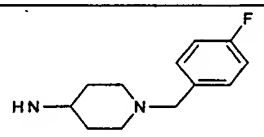
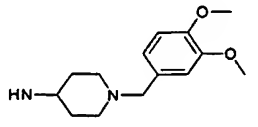
(I)

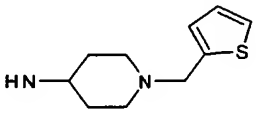
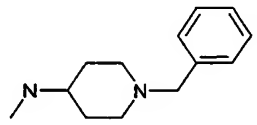
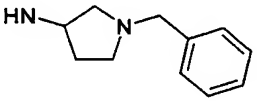
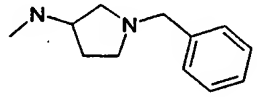
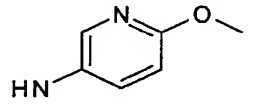
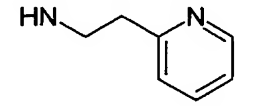
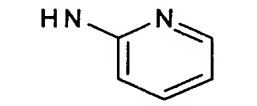
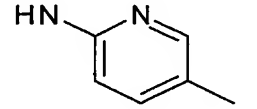
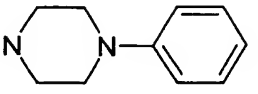
Compounds of formula (I) wherein R^3 = H:

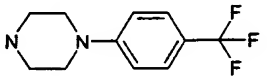
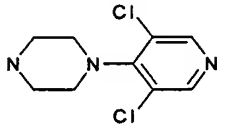
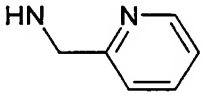
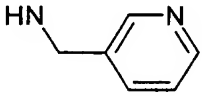
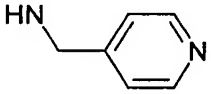
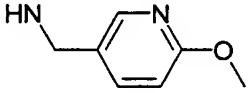
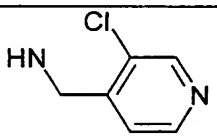
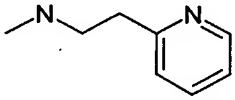
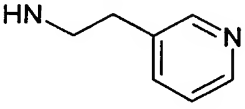
R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
1	43	76	106	133	
2	44	77	107	134	
3	45	78	108	135	
4	46	79	109	-	
5	-	-	-	-	
6	47	80	110	136	

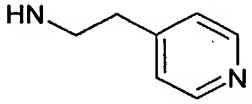
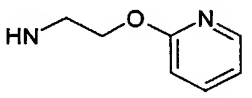
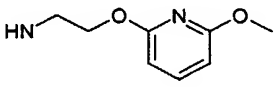
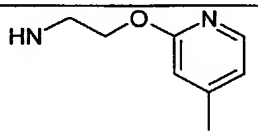
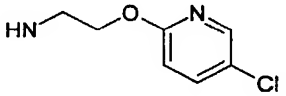
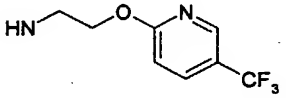
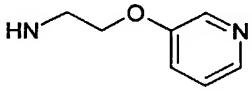
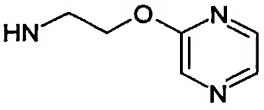
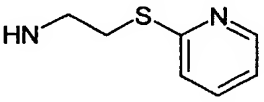
R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
7	48	81	111	137	
8	49	82	112	138	
9	50	83	113	139	
10	51	84	114	140	
11	52	85	115	141	
12	53	86	116	142	
13	54	87	117	143	
14	55	88	118	144	
15	56	89	119	145	

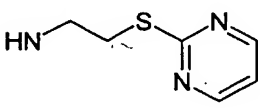
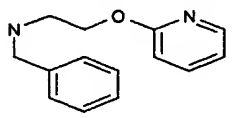
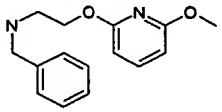
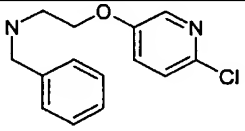
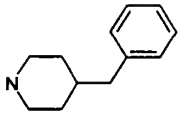
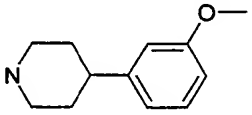
R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
16	57	-	120	-	
17	58	90	121	146	
18	59	91	122	147	
19	60	92	123	148	
20	61	93	-	149	
21	-	-	-	150	
22	62	94	124	151	
-	63	95	-	152	
23	-	-	-	-	

R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
24	64	-	-	153	
25	-	-	-	-	
26	65	-	125	154	
-	66	-	-	155	
27	67	96	126	156	
28	-	-	-	-	
29	68	97	127	157	
30	69	98	128	158	
31	70	99	129	159	

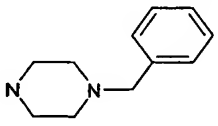
R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
32	71	100	130	160	
33	72	101	131	161	
34	73	102	-	-	
35	74	-	-	-	
36	-	103	-	-	
37	75	104	132	162	
38	-	105	-	-	
39	-	-	-	-	
40	-	-	-	-	

R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
41	-	-	-	-	
42	-	-	-	-	
164	186	-	196	204	
165	187	-	197	205	
166	188	-	-	206	
167	189	-	198	207	
168	-	-		208	
169	190	195	199	209	
170	191	-	200	210	

R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
171	192	-	201	211	
172	193	-	202	212	
173	-	-	-	-	
174	-	-	-	-	
175	-	-	-	-	
176	-	-	-	-	
177	-	-	-	-	
178	-	-	-	-	
179	-	-	-	-	

R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
180	-	-	-	-	
181	194	-	-203		
182	-	-	-	-	
183	-	-	-	-	
184	-	-	-	-	
185	-	-	-	-	

Compounds of formula (I) wherein R^3 = Cl:

R^1 = Me R^2 = Me	R^1 = Et R^2 = Et	R^1 = *n*Pro R^2 = *n*Pro	R^1 = *n*Pro R^2 = Me	R^1 = Me R^2 = *n*Pro	R^1R^2 / NR^4R^5
163	-	-	-	-	

5

EXAMPLE 1

6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

To a mixture of the title compound of Preparation 1 (0.1 g, 0.28 mmol) and triethylamine (0.043 ml, 0.31 mmol) in dichloromethane (5 ml) was added 1-benzylpiperazine (0.054 ml, 0.31 mmol) and the resulting mixture was stirred at room temperature overnight. The reaction mixture was diluted with dichloromethane, washed with an aqueous solution of sodium bicarbonate in water, dried ($MgSO_4$) and evaporated under reduced pressure. The resulting crude residue was triturated with diethylether and the precipitate collected by filtration and dried under vacuum to yield the title compound (65 mg, 47%).
ESI/MS m/e: 494 ($[M+H]^+$, $C_{25}H_{27}N_5O_4S$)

Retention Time (min.): 6.6

EXAMPLES 2-42 and 164-185

These compounds were synthesized from the title compound of Preparation 1 following the procedure of example 1 and using the corresponding reactant. The ESI/MS data, HPLC retention times and yields are summarised in Table 4.

TABLE 4

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
2	$C_{25}H_{26}FN_5O_4S$	512	6.5	52
3	$C_{25}H_{26}FN_5O_4S$	512	7.2	35
4	$C_{25}H_{25}F_2N_5O_4S$	530	7.5	44
5	$C_{25}H_{26}FN_5O_4S$	512	6.9	85
6	$C_{25}H_{26}ClN_5O_4S$	528	7.4	70
7	$C_{25}H_{26}ClN_5O_4S$	528	7.9	70
8	$C_{25}H_{26}BrN_5O_4S$	572	7.7	50
9	$C_{25}H_{26}BrN_5O_4S$	573	8.8	56

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
10	$C_{26}H_{26}F_3N_5O_4S$	562	8.6	74
11	$C_{29}H_{35}N_5O_4S$	550	8.0	35
12	$C_{26}H_{29}N_5O_5S$	524	5.9	65
13	$C_{26}H_{29}N_5O_5S$	524	6.3	62
14	$C_{26}H_{27}N_5O_6S$	538	6.5	58
15	$C_{26}H_{26}N_6O_4S$	519	7.2	58
16	$C_{23}H_{25}N_5O_5S$	484	5.5	29
17	$C_{23}H_{25}N_5O_4S_2$	500	6.6	80
18	$C_{23}H_{24}ClN_5O_4S_2$	535	8.9	84
19	$C_{24}H_{26}N_6O_4S$	495	5.8	26
20	$C_{26}H_{29}N_5O_4S$	508	6.2	50
21	$C_{26}H_{29}N_5O_4S$	508	5.8	54
22	$C_{26}H_{28}FN_5O_4S$	526	6.3	59
23	$C_{27}H_{29}N_5O_4S$	520	6.5	58
24	$C_{26}H_{27}N_5O_4S$	506	5.6	64
25	$C_{31}H_{31}N_5O_4S$	570	10.7	66
26	$C_{24}H_{27}N_5O_4S$	482	5.9	62
27	$C_{23}H_{24}N_6O_4S$	481	7.1	58
28	$C_{23}H_{25}N_7O_5S$	512	6.6	63
29	$C_{26}H_{29}N_5O_4S$	508	5.8	44
30	$C_{26}H_{28}FN_5O_4S$	526	5.9	60
31	$C_{28}H_{33}N_5O_6S$	566	5.4	49
32	$C_{24}H_{27}N_5O_4S_2$	514	5.3	54
33	$C_{27}H_{31}N_5O_4S$	522	6.0	47
34	$C_{25}H_{27}N_5O_4S$	494	5.5	72
35	$C_{26}H_{29}N_5O_4S$	508	5.7	74
36	$C_{20}H_{19}N_5O_5S$	442	8.0	84
37	$C_{21}H_{21}N_5O_4S$	440	5.5	54
38	$C_{19}H_{17}N_5O_4S$	412	6.6	52

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
39	$C_{20}H_{19}N_5O_4S$	526	6.4	24
40	$C_{24}H_{25}N_5O_4S$	480	9.4	81
41	$C_{25}H_{24}F_3N_5O_4S$	548	10.2	26
42	$C_{23}H_{22}Cl_2N_6O_4S$	550	9.5	48
164	$C_{20}H_{19}N_5O_4S$	426	6.4	45
165	$C_{20}H_{19}N_5O_4S$	426	5.7	82
166	$C_{20}H_{19}N_5O_4S$	426	5.3	44
167	$C_{21}H_{21}N_5O_5S$	456	7.2	52
168	$C_{20}H_{18}ClN_5O_4S$	461	7.3	25
169	$C_{22}H_{23}N_5O_4S$	455	6.0	15
170	$C_{21}H_{21}N_5O_4S$	440	5.4	58
171	$C_{21}H_{21}N_5O_4S$	440	5.1	65
172	$C_{21}H_{21}N_5O_5S$	456	7.3	66
173	$C_{22}H_{23}N_5O_6S$	487	8.1	89
174	$C_{22}H_{23}N_5O_5S$	471	7.6	90
175	$C_{21}H_{20}ClN_5O_5S$	491	8.3	91
176	$C_{22}H_{20}F_3N_5O_5S$	524	8.5	65
177	$C_{21}H_{21}N_5O_5S$	456	5.8	85
178	$C_{20}H_{20}N_6O_5S$	457	6.9	68
179	$C_{21}H_{21}N_5O_4S_2$	473	7.8	75
180	$C_{20}H_{20}N_6O_4S_2$	474	7.1	65
181	$C_{28}H_{27}N_5O_5S$	547	9.3	44
182	$C_{29}H_{29}N_5O_6S$	577	10.1	74
183	$C_{28}H_{26}ClN_5O_5S$	581	9.4	74

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
184	$C_{26}H_{28}N_4O_4S$	494	9.8	54
185	$C_{26}H_{28}N_4O_5S$	510	9.3	49

(Example 172) δ ^{1}H NMR (DMSO): 12.65 (bs, 1H), 8.18 (d, 2H), 7.95 (t, 1H), 7.82 (d, 2H), 7.66 (dd, 1H), 6.98 (t, 1H), 6.9 (s, 1H), 6.75 (d, 1H), 4.22 (t, 2H), 3.43 (s, 3H), 3.25 (s, 3H), 3.21 (q, 2H).

(Example 173) δ ^{1}H NMR (DMSO): 8.05 (d, 2H), 7.85 (d, 2H), 7.50 (t, 1H), 6.90 (s, 1H), 6.25 (t, 2H), 4.20 (m, 2H), 3.80 (s, 3H), 3.45 (s, 3H), 3.35 (m, 2H), 3.15 (s, 3H), 3.05 (s, 3H).

EXAMPLES 43-75 and 186-194

These compounds were synthesized from the title compound of Preparation 2 following the procedure of example 1 and using the corresponding reactant. The ESI/MS data, HPLC retention times and yields are summarised in Table 5.

TABLE 5

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
43	$C_{27}H_{31}N_5O_4S$	522	7.1	20
44	$C_{27}H_{30}FN_5O_4S$	540	7.5	70
45	$C_{27}H_{30}FN_5O_4S$	540	8.3	62
46	$C_{27}H_{29}F_2N_5O_4S$	558	8.6	65
47	$C_{27}H_{30}ClN_5O_4S$	556	8.6	48
48	$C_{27}H_{30}ClN_5O_4S$	556	9.1	77
49	$C_{27}H_{30}BrN_5O_4S$	601	8.9	76
50	$C_{27}H_{30}BrN_5O_4S$	601	9.9	63
51	$C_{28}H_{30}F_3N_5O_4S$	590	9.6	60

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
52	$C_{31}H_{39}N_5O_4S$	578	8.9	58
53	$C_{28}H_{33}N_5O_5S$	552	6.7	70
54	$C_{28}H_{33}N_5O_5S$	552	7.2	36
55	$C_{28}H_{31}N_5O_6S$	566	6.9	44
56	$C_{28}H_{30}N_6O_4S$	547	8.3	50
57	$C_{25}H_{29}N_5O_5S$	512	6.3	50
58	$C_{25}H_{29}N_5O_4S_2$	528	7.7	66
59	$C_{25}H_{28}ClN_5O_4S_2$	562	9.8	74
60	$C_{26}H_{30}N_6O_4S$	523	6.7	39
61	$C_{28}H_{33}N_5O_4S$	536	7.0	28
62	$C_{28}H_{32}FN_5O_4S$	554	6.6	80
63	$C_{28}H_{33}N_5O_4S$	536	6.8	62
64	$C_{28}H_{31}N_5O_4S$	534	6.2	57
65	$C_{26}H_{31}N_5O_4S$	510	6.2	47
66	$C_{27}H_{33}N_5O_5S$	540	6.2	60
67	$C_{25}H_{28}N_6O_4S$	509	7.8	56
68	$C_{28}H_{33}N_5O_4S$	536	6.1	70
69	$C_{28}H_{32}FN_5O_4S$	554	6.2	63
70	$C_{30}H_{37}N_5O_6S$	596	6.0	51
71	$C_{26}H_{31}N_5O_4S_2$	542	6.0	74
72	$C_{29}H_{35}N_5O_4S$	550	6.3	38
73	$C_{27}H_{31}N_5O_4S$	522	6.0	32
74	$C_{28}H_{33}N_5O_4S$	536	6.3	87
75	$C_{23}H_{25}N_5O_4S$	468	6.5	36
186	$C_{22}H_{23}N_5O_4S$	455	7.4	54
187	$C_{22}H_{23}N_5O_4S$	455	6.7	86
188	$C_{22}H_{23}N_5O_4S$	455	6.2	85
189	$C_{23}H_{25}N_5O_5S$	485	8.1	75

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
190	$C_{24}H_{27}N_5O_4S$	483	7.0	74
191	$C_{23}H_{25}N_5O_4S$	469	6.3	61
192	$C_{23}H_{25}N_5O_4S$	469	6.0	80
193	$C_{23}H_{25}N_5O_5S$	485	8.2	58
194	$C_{30}H_{31}N_5O_5S$	575	9.9	65

EXAMPLES 76-105 and 195

These compounds were synthesized from the title compound of Preparation 3 following the procedure of example 1 and using the corresponding reactant. The ESI/MS data, HPLC retention times and yields are summarised in Table 6.

TABLE 6

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
76	$C_{29}H_{35}N_5O_4S$	550	8.4	60
77	$C_{29}H_{34}FN_5O_4S$	568	8.7	74
78	$C_{29}H_{34}FN_5O_4S$	568	9.5	90
79	$C_{29}H_{33}F_2N_5O_4S$	586	9.7	58
80	$C_{29}H_{34}ClN_5O_4S$	586	9.9	57
81	$C_{29}H_{34}ClN_5O_4S$	585	10.2	39
82	$C_{29}H_{34}BrN_5O_4S$	629	10.1	58
83	$C_{29}H_{34}BrN_5O_4S$	629	10.8	64
84	$C_{30}H_{34}F_3N_5O_4S$	618	10.5	68
85	$C_{33}H_{43}N_5O_4S$	606	10.1	75
86	$C_{30}H_{37}N_5O_5S$	580	7.7	49
87	$C_{30}H_{37}N_5O_5S$	580	8.4	31

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
88	$C_{30}H_{35}N_5O_6S$	594	7.9	54
89	$C_{30}H_{34}N_6O_4S$	575	9.4	52
90	$C_{27}H_{33}N_5O_4S_2$	556	9.0	61
91	$C_{27}H_{32}ClN_5O_4S_2$	592	10.6	25
92	$C_{28}H_{34}N_6O_4S$	551	7.9	74
93	$C_{30}H_{37}N_5O_4S$	564	8.2	52
94	$C_{30}H_{36}FN_5O_4S$	582	7.4	70
95	$C_{30}H_{37}N_5O_4S$	564	7.8	69
96	$C_{27}H_{32}N_6O_4S$	537	9.0	33
97	$C_{30}H_{37}N_5O_4S$	564	6.9	30
98	$C_{30}H_{36}FN_5O_4S$	582	6.9	55
99	$C_{32}H_{41}N_5O_6S$	624	6.8	80
100	$C_{28}H_{35}N_5O_4S_2$	570	6.7	77
101	$C_{31}H_{39}N_5O_4S$	578	7.1	29
102	$C_{29}H_{35}N_5O_4S$	550	6.8	38
103	$C_{24}H_{27}N_5O_5S$	498	9.2	49
104	$C_{25}H_{29}N_5O_4S$	496	7.8	54
105	$C_{23}H_{25}N_5O_4S$	468	8.1	66
195	$C_{26}H_{31}N_5O_4S$	511	8.4	71

EXAMPLES 106-132 and 196-203

These compounds were synthesized from the title compound of Preparation 4 following the procedure of example 1 and using the corresponding reactant. The ESI/MS data, HPLC retention times and yields are summarised in Table 7.

TABLE 7

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
106	$C_{27}H_{31}N_5O_4S$	522	7.2	70
107	$C_{27}H_{30}FN_5O_4S$	540	7.6	66
108	$C_{27}H_{30}FN_5O_4S$	540	8.2	29
109	$C_{27}H_{29}F_2N_5O_4S$	558	8.5	27
110	$C_{27}H_{30}ClN_5O_4S$	557	8.6	35
111	$C_{27}H_{30}ClN_5O_4S$	556	9.2	57
112	$C_{27}H_{30}BrN_5O_4S$	601	8.9	84
113	$C_{27}H_{30}BrN_5O_4S$	601	9.9	48
114	$C_{28}H_{30}F_3N_5O_4S$	590	9.6	41
115	$C_{31}H_{39}N_5O_4S$	578	8.9	32
116	$C_{28}H_{33}N_5O_5S$	552	6.7	58
117	$C_{28}H_{33}N_5O_5S$	552	7.3	51
118	$C_{28}H_{31}N_5O_6S$	566	6.9	55
119	$C_{28}H_{30}N_6O_4S$	547	8.3	64
120	$C_{25}H_{29}N_5O_5S$	512	6.3	35
121	$C_{25}H_{29}N_5O_4S_2$	528	7.7	48
122	$C_{25}H_{28}ClN_5O_4S_2$	563	9.8	54
123	$C_{26}H_{30}N_6O_4S$	523	6.7	59
124	$C_{28}H_{32}FN_5O_4S$	554	6.6	65
125	$C_{26}H_{31}N_5O_4S$	510	6.3	80
126	$C_{25}H_{28}N_6O_4S$	509	7.8	47
127	$C_{28}H_{33}N_5O_4S$	536	6.1	81
128	$C_{28}H_{32}FN_5O_4S$	554	6.3	56
129	$C_{30}H_{37}N_5O_6S$	596	6.1	63
130	$C_{26}H_{31}N_5O_4S_2$	542	6.1	65
131	$C_{29}H_{35}N_5O_4S$	550	6.4	68
132	$C_{23}H_{25}N_5O_4S$	468	6.6	64

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
196	$C_{22}H_{23}N_5O_4S$	455	7.4	85
197	$C_{22}H_{23}N_5O_4S$	455	6.8	84
198	$C_{23}H_{25}N_5O_5S$	485	8.1	66
199	$C_{24}H_{27}N_5O_4S$	483	7.1	91
200	$C_{23}H_{25}N_5O_4S$	469	6.4	45
201	$C_{23}H_{25}N_5O_4S$	469	6.0	30
202	$C_{23}H_{25}N_5O_5S$	485	8.2	57
203	$C_{30}H_{31}N_5O_5S$	575	10.0	66

EXAMPLES 133-162 and 204-212

These compounds were synthesized from the title compound of Preparation 5 following the procedure of example 1 and using the corresponding reactant. The ESI/MS data, HPLC retention times and yields are summarised in Table 8.

TABLE 8

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
133	$C_{27}H_{31}N_5O_4S$	522	7.3	45
134	$C_{27}H_{30}FN_5O_4S$	540	7.5	49
135	$C_{27}H_{30}FN_5O_4S$	540	8.5	58
136	$C_{27}H_{30}ClN_5O_4S$	556	8.8	84
137	$C_{27}H_{30}ClN_5O_4S$	556	9.3	29
138	$C_{27}H_{30}BrN_5O_4S$	601	9.0	28
139	$C_{27}H_{30}BrN_5O_4S$	601	10.0	56
140	$C_{28}H_{30}F_3N_5O_4S$	590	9.7	45

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
141	$C_{31}H_{39}N_5O_4S$	578	9.1	54
142	$C_{28}H_{33}N_5O_5S$	552	6.8	48
143	$C_{28}H_{33}N_5O_5S$	552	7.4	50
144	$C_{28}H_{31}N_5O_6S$	566	7.1	72
145	$C_{28}H_{30}N_6O_4S$	547	8.4	77
146	$C_{25}H_{29}N_5O_4S_2$	528	7.8	66
147	$C_{25}H_{28}ClN_5O_4S_2$	562	9.8	36
148	$C_{26}H_{30}N_6O_4S$	523	6.8	39
149	$C_{28}H_{33}N_5O_4S$	536	7.1	47
150	$C_{28}H_{33}N_5O_4S$	536	6.5	78
151	$C_{28}H_{32}FN_5O_4S$	554	6.7	59
152	$C_{28}H_{33}N_5O_4S$	536	6.9	66
153	$C_{28}H_{31}N_5O_4S$	534	6.3	60
154	$C_{26}H_{31}N_5O_4S$	510	6.3	69
155	$C_{27}H_{33}N_5O_5S$	540	6.3	49
156	$C_{25}H_{28}N_6O_4S$	509	7.8	75
157	$C_{28}H_{33}N_5O_4S$	536	6.2	38
158	$C_{28}H_{32}FN_5O_4S$	554	6.2	24
159	$C_{30}H_{37}N_5O_6S$	596	6.0	62
160	$C_{26}H_{31}N_5O_4S_2$	542	6.0	50
161	$C_{29}H_{35}N_5O_4S$	550	6.4	47
162	$C_{23}H_{25}N_5O_4S$	468	6.6	58
204	$C_{22}H_{23}N_5O_4S$	455	7.5	45
205	$C_{22}H_{23}N_5O_4S$	455	6.9	58
206	$C_{22}H_{23}N_5O_4S$	455	6.4	91
207	$C_{23}H_{25}N_5O_5S$	485	8.2	75
208	$C_{22}H_{22}ClN_5O_4S$	489	8.2	71
209	$C_{24}H_{27}N_5O_4S$	483	7.2	84

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
210	$C_{23}H_{25}N_5O_4S$	469	6.4	58
211	$C_{23}H_{25}N_5O_4S$	469	6.0	66
212	$C_{23}H_{25}N_5O_5S$	485	8.3	62

EXAMPLE 163

This compound was synthesized from the title compound of Preparation 6 and from 1-benzylpiperazine following the procedure of example 1.

ESI/MS m/e: 529 ($[M+H]^+$, $C_{25}H_{26}ClN_5O_4S$)

Retention Time (min.): 7.4

The following examples illustrate pharmaceutical compositions according to the present invention and procedure for their preparation.

COMPOSITION EXAMPLE 1

50,000 capsules each containing 100 mg of 3-methyl-6- [5-(4-methylpiperazine-1-sulphonyl)-2-propoxyphenyl]-1-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione (active ingredient) were prepared according to the following formulation:

Active ingredient	5 Kg
Lactose monohydrate	10 Kg
Colloidal silicon dioxide	0.1 Kg
Corn starch	1 Kg
Magnesium stearate	0.2 Kg

Procedure

The above ingredients were sieved through a 60 mesh sieve, and were loaded into a suitable mixer and filled into 50,000 gelatine capsules.

COMPOSITION EXAMPLE 2

50,000 tablets each containing 50 mg of 6-[5-(4-ethylpiperazine-1-sulphonyl)-2-propoxyphenyl]-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione (active ingredient) were prepared from the following formulation:

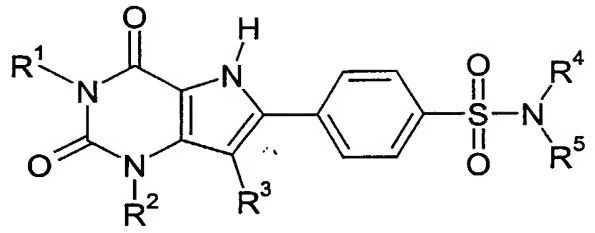
Active ingredient	2.5 Kg
Microcrystalline cellulose	1.95 Kg
Spray dried lactose	9.95 Kg
Carboxymethyl starch	0.4 Kg
Sodium stearyl fumarate	0.1 Kg
Colloidal silicon dioxide	0.1 Kg

Procedure

All the powders were passed through a screen with an aperture of 0.6 mm, then mixed in a suitable mixer for 20 minutes and compressed into 300 mg tablets using 9 mm disc and flat bevelled punches. The disintegration time of the tablets was about 3 minutes.

CLAIMS

1. A compound of formula (I)



(I)

wherein

R^1 and R^2 each independently represent:

a hydrogen atom;

a hydrocarbon chain selected from an alkyl, alkenyl or alkynyl group, which is optionally substituted by one or more substituents selected from halogen, hydroxy, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, cyano, oxo, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy or dialkoxyphosphoryloxy groups;

or a group of formula

$$-(CH_2)_n-R^6$$

wherein n is an integer from 0 to 4 and R^6 represents a 3- to 7-membered aromatic or non-aromatic cyclic group containing from 0 to 4 heteroatoms selected from N, O and S, which is optionally bridged and/or fused to another 3- to 7-membered aromatic or non-aromatic cyclic group containing from 0 to 4 heteroatoms selected from N, O and S;

the cyclic groups in the moiety R^6 being optionally substituted by one or more R^7 substituents selected from halogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino,

monoalkylamino, dialkylamino, nitro, cyano, oxo, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy and dialkoxyphosphoryloxy groups;

the hydrocarbon chains and the cyclic moieties of these R^7 substituents being optionally substituted by one or more further R^8 substituents selected from halogen, hydroxy, oxo, cyano, alkyl, difluoromethyl, trifluoromethyl, alkoxy, alkylenedioxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, monoalkylamino, dialkylamino and hydroxycarbonyl groups;

R^3 represents a hydrogen or halogen atom, or a nitro, alkoxycarbonyl or alkyl group; the alkyl group being optionally substituted by one or more substituents selected from hydroxy, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl or alkylcarbamoyl groups;

R^4 and R^5 are the same or different, each independently representing:

hydrogen;

a group of formula $-(CH_2)_n-R^6$; wherein n is an integer from 0 to 4; and R^6 is as defined above and is optionally substituted by one or more R^7 substituents, wherein R^7 is as defined above and is optionally substituted by one or more further R^8 substituents, wherein R^8 is as defined above;

or a hydrocarbon chain selected from alkyl, alkenyl or alkynyl, which is optionally substituted by one or more substituents selected from $-(CH_2)_n-R^6$, $-O-(CH_2)_n-R^6$, $-S-(CH_2)_n-R^6$, $-NH-(CH_2)_n-R^6$, hydroxy, oxo, halogen, alkoxy, alkylthio, amino, monoalkylamino, and dialkylamino groups; the alkyl chains in the alkoxy, alkylthio, monoalkylamino and dialkylamino substituents being optionally substituted by one or more further substituents selected from $-(CH_2)_n-R^6$, hydroxy, oxo, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; wherein each n is independently an integer from 0 to 4 and each R^6 is as defined above and is optionally substituted by one or more R^7 substituents, wherein R^7 is as defined above and is optionally substituted by one or more further R^8 substituents, wherein R^8 is as defined above;

or, alternatively, R^4 and R^5, together with the nitrogen atom to which they are attached, form a 3- to 7-membered aromatic or non-aromatic cyclic group containing from 1 to 4 heteroatoms selected from N, O and S, which is optionally bridged and/or fused to another 3- to 7-membered aromatic or non-aromatic cyclic group containing from 0 to 4 heteroatoms selected from N, O and S; the cyclic groups being optionally substituted by one or more substituents selected from $-(CH_2)_n-R^6$ and R^7; the hydrocarbon chains and the cyclic moieties of the R^7 substituents being optionally substituted by one or more further substituents selected from $-(CH_2)_n-R^6$ and R^8; and the alkyl chains in the R^8 substituents being optionally substituted by one or more further substitutents selected from $-(CH_2)_n-R^6$, hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; wherein each of the R^6 substituents is optionallly substitued by one or more R^7 substituents and each of these R^7 substituents is optionally substituted by one or more R^8 substituents; and wherein each n, R^6, R^7 and R^8 is as defined above;

or an N-oxide or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein each of R^1 and R^2 independently represents:

an alkyl group optionally substituted by one or more substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino, dialkylamino, hydroxycarbonyl, and alkoxycarbonyl groups;

or a group of formula $-(CH_2)_n-R^6$, wherein n is an integer from 0 to 2 and R^6 represents a 3- to 7-membered aromatic or non-aromatic cyclic group having from 0 to 2 heteroatoms selected from nitrogen and oxygen.

3. A compound according to claim 2 wherein R^1 and R^2 are both unsubstituted C_1-C_6 alkyl groups.

4. A compound according to any one of the preceding claims wherein R^3 represents hydrogen or a halogen atom.

5. A compound according to any one of the preceding claims wherein R^4 is as defined in claim 1 and R^5 is hydrogen, a group of formula $-(CH_2)_n-R^6$ or a hydrocarbon chain selected

from alkyl, alkenyl and alkynyl, which is optionally substituted by one or more groups selected from $-(CH_2)_n-R^6$ and $-(CH_2)_n-O-R^6$; each R^6 being a phenyl or a pyridyl group which is optionally substituted by one or more substituents selected from halogen, hydroxy, alkyl, alkoxy and alkylthio groups.

6. A compound according to claim 5, wherein R^5 is hydrogen or an alkyl group.

7. A compound according to any one of claims 5 or 6, wherein R^4 is

- hydrogen;

- a group of formula $-(CH_2)_n-R^6$ wherein n is 0, 1 or 2 and R^6 is a 5- to 6- membered heteroaryl or heterocyclyl group containing up to 2 heteroatoms selected from N, O and S, which is optionally substituted by a R^7 substituent selected from alkyl, alkoxy, arylalkyl or heteroarylalkyl groups, the aryl and heteroaryl moieties of these arylalkyl and heteroarylalkyl R^7 substituents being optionally substituted by 1 or 2 further R^8 substituents selected from halogen, cyano, alkyl, trifluoromethyl, alkoxy and alkylenedioxy; or

- an alkyl group which is optionally substituted by 1 or 2 substituents selected from amino, monoalkylamino, dialkylamino, $-OR^6$ and $-SR^6$ substituents, wherein R^6 is a 5- or 6-membered heteroaryl group containing 1 or 2 heteroatoms, and is optionally substituted by one or more R^7 substituents selected from hydroxy, halogen, amino, monoalkylamino, dialkylamino, cyano, hydroxycarbonyl, alkoxycarbonyl, alkoxy, alkylenedioxy and alkylthio; and wherein the alkyl chains of each of the said monoalkylamino and dialkylamino substituents are optionally substituted by 1 or 2 further substituents selected from a hydroxy group and a group of formula $-(CH_2)_n-R^6$, wherein n is an integer from 0 to 4 and R^6 is an aryl group.

8. A compound according to any one of claims 1 to 4 wherein R^4 and R^5 form, together with the nitrogen atom to which they are attached, an optionally bridged 5- to 7-membered aromatic or non-aromatic cyclic group which contains up to two nitrogen atoms, and which is optionally substituted by a group of formula $-(CH_2)_n-R^6$ or by a R^7 substituent selected from alkyl, alkenyl and alkynyl chains; the said alkyl, alkenyl and alkynyl chains being optionally substituted by one or more groups of formula $-(CH_2)_n-R^6$ or R^8 substituents

selected from hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino, and dialkylamino groups; the alkyl chains in these R^8 substituents being optionally substituted by one or more further substituents selected from a group of formula $-(CH_2)_n-R^6$, and hydroxy, halogen, alkoxy, alkylthio, amino, monoalkylamino and dialkylamino groups; wherein each of the R^6 groups is optionallly substitued by one or more R^7 substituents and each of these R^7 substituents is optionally substituted by one or more R^8 substituents; each n, R^6, R^7 and R^8 being as defined in claim 1.

9. A compound according to claim 8 wherein R^4 and R^5 form, together with the N atom to which they are attached, a 5-, 6- or 7- membered saturated heterocyclic group which contains 1 or 2 nitrogen atoms and which optionally carries a bridging alkylene group, said cyclic group being optionally substituted by a group of formula $-(CH_2)_n-R^6$ wherein n is 0, 1 or 2 and R^6 is a 5- or 6- membered aromatic or non-aromatic ring containing 0, 1 or 2 heteroatoms selected from N, O and S, or by a R^7 substituent selected from alkyl and alkenyl groups, the group R^6 being optionally substituted by 1, 2 or 3 further substituents selected from haloalkyl, alkyl, alkoxy, alkylenedioxy, cyano and halogen groups, and the said R^7 substituent being optionally substituted by 1 or 2 phenyl substituents.

10. A compound according to claim 1 which is one of

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(pyridin-2-yloxy)ethyl]benzenesulfonamide
4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[2-(6-methoxypyridin-2-yloxy)ethyl]benzenesulfonamide
6-[4-(4-Benzylpiperazine-1-sulphonyl)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione
6-{4-[4-(4-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione
6-[4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulphonyl)phenyl]-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione
6-{4-[4-(3-Fluorobenzyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione
1-Methyl-3-propyl-6-[4-(4-pyridin-2-ylpiperazine-1-sulphonyl)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulphonamide

4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(2-pyridin-2-ylethyl)benzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-pyridin-2-ylbenzenesulphonamide

4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(6-methoxypyridin-3-yl)benzenesulphonamide

6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

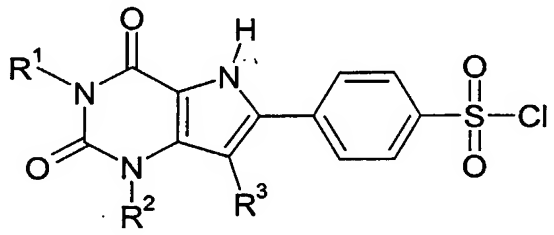
6-{4-[4-(5-Chlorothiophen-2-ylmethyl)piperazine-1-sulphonyl]phenyl}-1,3-diethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(1-Benzylpiperidin-4-yl)-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzenesulphonamide

4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-[1-(4-fluorobenzyl)piperidin-4-yl]benzenesulphonamide

or a pharmaceutically acceptable salt or an N-oxide thereof.

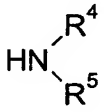
11. A process for producing a compound of formula I as defined in any one of claims 1 to 10, which process comprises reacting a sulphonyl chloride of formula II



(II)

wherein R^1, R^2 and R^3 are as defined in any one of claims 1 to 4 or 10,

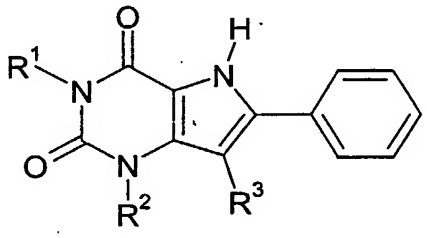
with the corresponding amine III



(III)

wherein R^4 and R^5 are as defined in any one of claims 1 or 5 to 10.

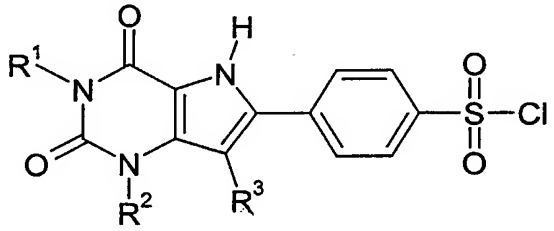
12. A process according to claim 11, wherein the sulphonyl chloride of formula II is obtained from the corresponding compound of formula IV:



(IV)

wherein R^1, R^2 and R^3 are as defined in any one of claims 1 to 4 or 10, by reaction with an excess of chlorosulphonic acid.

13. A compound of formula II



(II)

wherein R^1, R^2 and R^3 are as defined in any one of claims 1 to 4 or 10.

14. A compound according to any one of claims 1 to 10 for use in the treatment of a pathological condition or disease susceptible to amelioration by antagonism of adenosine A_{2A} and/or A_{2B} receptors.

15. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 10 mixed with a pharmaceutically acceptable diluent or carrier.

16. Use of a compound as defined in any one of claims 1 to 10 in the manufacture of a medicament for the treatment of a pathological condition or disease susceptible of being improved by antagonism of A_{2A} and/or A_{2B} adenosine receptors.

17. Use according to claim 16, wherein the pathological condition or disease is Parkinson´s disease, Alzheimer disease, Huntington chorea, Wilson's disease, asthma, bronchoconstriction, allergic diseases, hypertension, atherosclerosis, reperfusion injury, myocardial ischemia, retinopathy, inflammation, gastrointestinal tract disorders, cell proliferation disorders, diabetes mellitus, and/or autoimmune diseases.

18. A method for treating a subject afflicted with a pathological condition or disease susceptible to amelioration by antagonism of A_{2A} and/or A_{2B} adenosine receptors, which comprises administering to said subject an effective amount of a compound as defined in any one of claims 1 to 10.

19. A method according to claim 18, wherein the pathological condition or disease is Parkinson´s disease, Alzheimer disease, Huntington chorea, Wilson's disease, asthma, bronchoconstriction, allergic diseases, hypertension, atherosclerosis, reperfusion injury, myocardial ischemia, retinopathy, inflammation, gastrointestinal tract disorders, cell proliferation disorders, diabetes mellitus, and/or autoimmune diseases.

INTERNATIONAL SEARCH REPORT

Intern pplication No
PCT/ER 03/03378

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D487/04 A61K31/519 A61P25/00 A61P11/06 A61P37/08
A61P9/12 A61P1/00 //(C07D487/04,239:00,209:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 092 398 A (WARNER LAMBERT CO) 26 October 1983 (1983-10-26) page 10, line 9 -page 12, line 16; claim 1	1,14,17
A	WO 01 94350 A (ALMIRALL PRODESFARMA) 13 December 2001 (2001-12-13) claims 1,20	1,17
P,X	WO 03 000694 A (ALMIRALL PRODESFARMA) 3 January 2003 (2003-01-03) page 1, paragraph 1; claims 1,24	1,14,17

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 June 2003	24/06/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Alfaro Faus, I

INTERNATIONAL SEARCH REPORT

Int ...nal application No.
...CT/EP 03/03378

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 18 and 19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Inter Application No
PCT/EP 03/03378

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